Original article

Nuclear Medicine Communications

The value of ^{99m}Tc-MDP bone SPECT/CT in evaluation of patients with painful knee prosthesis

Ramin Mandegaran[a], Kanhaiyalal Agrawal[a,c], Sanjay Vijayanathan[a] and Gopinath Gnanasegaran[a,b]

Objective **The purpose of this study was to assess the incremental value of technetium-99m-methyl diphosphonate (^{99m}Tc-MDP) single-photon emission computed tomography/computed tomography (SPECT/CT) over ^{99m}Tc-MDP two-phase bone scan (TPBS) in the assessment of the patients with pain following knee arthroplasty.**

Patients and methods **^{99m}Tc-MDP TPBS and ^{99m}Tc-MDP SPECT/CT were performed in 49 patients with knee pain after knee arthroplasty. The scans were reviewed by two readers (nuclear medicine physician and musculoskeletal radiologist). ^{99m}Tc-MDP SPECT/CT studies were interpreted in conjunction with TPBS in this retrospective study to identify the pain generator in painful knee prosthesis. The final diagnosis was established based on a combination of histopathological/cytological findings, other imaging findings (e.g. MRI, radiolabelled white scan), clinical decisions, and management outcomes (including subsequent intraoperative findings).**

Results **In diagnosing infection or aseptic loosening, a definitive outcome regarding the presence/absence of aseptic loosening or periprosthetic infection was obtained in 41 patients. (a) Sensitivity of ^{99m}Tc-MDP SPECT/CT [100%; 95% confidence interval (CI): 66.4–100%] was higher than ^{99m}Tc-MDP TPBS (88.9%; 95% CI: 51.8–99.7%). (b) Specificity of ^{99m}Tc-MDP SPECT/CT (75%; 95% CI: 53.3–90.2%) was considerably higher than ^{99m}Tc-MDP TPBS (30%; 95% CI: 11.9–54.3%). Alternative diagnoses were identified in 21/49 (43%) patients on ^{99m}Tc-MDP SPECT/CT, which could not be ascertained on ^{99m}Tc-MDP TPBS alone.**

Conclusion **^{99m}Tc-MDP SPECT/CT has better sensitivity and specificity compared with ^{99m}Tc-MDP TPBS in diagnosis of aseptic loosening and periprosthestic infection in patients with painful knee arthroplasty. ^{99m}Tc-MDP SPECT/CT identified alternative causes of pain in 43% of patients, which was not identified by ^{99m}Tc-MDP TPBS.**

Nuclear Medicine Communications 2018, **39**:397–404

Keywords: bone scintigraphy, infection, knee arthroplasty, knee pain, loosening, single-photon emission computed tomography/computed tomography, knee arthroplasty

[a]Department of Nuclear Medicine, Guy's and St Thomas' NHS Foundation Trust, [b]Department of Nuclear Medicine, Royal Free London NHS Foundation Trust, London, UK and [c]Department of Nuclear Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

Correspondence to Kanhaiyalal Agrawal, MD, FABNM, MICNM, Department of Nuclear Medicine, All India Institute of Medical Sciences, Bhubaneswar 751019, Odisha, India
Tel: +91 819 593 0013; e-mail: drkanis@gmail.com

Received 13 December 2017 **Revised** 6 February 2018
Accepted 19 February 2018

Introduction

Knee arthroplasty (KA) represents one of the most commonly performed elective surgical procedures, typically performed in the context of knee arthropathy that significantly limits activities of daily living. Recent studies indicate that ~620 000 procedures are performed annually in the USA alone, with a prevalence of 1.52% among the US population [1,2]. Moreover, these figures are projected to increase rapidly over the coming years when accounting for trends of an ageing population, with annual procedures in the USA predicted to rise to 3.48 million by 2030 [3].

Although most patients experience significant improvement in quality of life following KA, a significant proportion (20–30%) are dissatisfied following surgery, often owing to pain, such that ~10% of patients will undergo some form of revision arthroplasty [1,4–8]. This large patient cohort has posed a significant diagnostic challenge as the possible etiologies of post-KA knee pain are vast (including aseptic loosening, infection, periprosthetic fracture, heterotopic ossification, component malalignment, and extensor mechanism pathology) with optimal management differing drastically depending on the cause [6,7,9,10]. Accurate detection of aseptic loosening and periprosthetic infection in particular are of paramount importance as these represent the two major indications for surgical management; the former often requiring revision arthroplasty, whereas the latter may involve a combination of irrigation and debridement with or without single-stage or two-stage exchange arthroplasty [9–11]. Diagnosis with conventional radiological modalities is challenging and frequently nonconclusive given the lack of metabolic information, compounded by image degradation secondary to metal artifacts [7,9,10,12,13].

DOI: 10.1097/MNM.0000000000000825

Scintigraphic techniques have long been used in conjunction to improve diagnostic accuracy, with two-phase or three-phase technetium-99m-methyl diphosphonate (^{99m}Tc-MDP) planar bone scans used to detect early metabolic changes of complications that may not be appreciable with conventional radiological modalities, although planar bone scans in isolation lack anatomical detail and specificity [7,10,14–16]. Often a three-phase bone scan is performed for diagnosis of infection in bone. However, in our practice, we have not found an effect of first phase of bone scan, that is, flow phase. Therefore, it is our institutional practice to do only two phases of bone scan, that is, blood pool and delayed phases for infection.

In recent years, ^{99m}Tc-MDP single-photon emission computed tomography/computed tomography (SPECT/CT) has been gaining favor in the assessment of the painful KA, with a growing number of studies demonstrating its clinical benefit owing to its ability to demonstrate anatomical, mechanical, and functional information simultaneously. However, despite its increasing use, no study has yet directly compared ^{99m}Tc-MDP SPECT/CT and ^{99m}Tc-MDP planar bone scans in the assessment of knee pain after KA. The purpose of this study was, therefore, to assess the incremental value of ^{99m}Tc-MDP SPECT/CT over ^{99m}Tc-MDP two-phase bone scan (TPBS) in the assessment of the patient with pain following KA, paying particular attention to (i) diagnostic accuracy in the identification of aseptic loosening and periprosthetic infection and (ii) additional diagnoses identified by performing ^{99m}Tc-MDP SPECT/CT.

Patients and methods

The retrospective data of all patients with knee pain following previous KA referred to our institution for ^{99m}Tc-MDP bone scan and also undergoing SPECT/CT of the knee between June 2006 and November 2013 were evaluated. The study was part of the SPECT/CT service evaluation audit and was approved by the institutional clinical governance committee. A total of 49 patients were identified with the following demographic profile: age 44–89 years (mean: 65.5 years) and 18 male and 31 female. The age of prosthesis at time of ^{99m}Tc-MDP SPECT/CT being performed was 4–184 months (mean: 46 months).

Data acquisition

Planar bone scintigraphy

^{99m}Tc-MDP of 800 MBq was injected intravenously. Planar bone scintigraphy was initially performed in all patients (two-phase images of both knees followed by whole body scan).

SPECT/CT images

SPECT/CT images were acquired using a Philips Precedence 16 system (Philips healthcare, Milpitas, California, USA). Low-energy high-resolution collimators were used. 128 projections of 20 s each over 360° on a 128×128 pixel matrix were acquired, with 100 mAs/slice at 120 kV and reconstructed using ordered subset expectation maximization (five iterations over eight subsets).

Image interpretation and analysis

^{99m}Tc-MDP TPBS studies were reviewed by two readers, a consultant nuclear medicine physician, and a dual-trained nuclear medicine and musculoskeletal consultant radiologist. ^{99m}Tc-MDP SPECT/CT studies were later interpreted in conjunction with the TPBS by the same two readers.

Given that aseptic loosening and periprosthetic infection represent the two major causes of painful knee prosthesis requiring revision surgery, a comparison was made between ^{99m}Tc-MDP TPBS and ^{99m}Tc-MDP SPECT/CT regarding the detection of either aseptic loosening or periprosthetic infection. For ^{99m}Tc-MDP TPBS interpretation, suspicion of periprosthetic infection was suggested by the combination increased blood pool activity on early images and increased periprosthetic uptake on the delayed images. Aseptic loosening was suggested by the combination of relatively normal blood pool activity and focal or linear delayed uptake relating to the periprosthetic margin or tip of the prosthetic stem. For ^{99m}Tc-MDP SPECT/CT interpretation, presence of periprosthetic infection was suggested as for ^{99m}Tc-MDP TPBS, with ancillary periprosthetic soft tissue features such as fluid collections, joint distension, inflammatory soft tissue edema, and fistulous tracts supporting the diagnosis. Similarly, presence of aseptic loosening on ^{99m}Tc-MDP SPECT/CT was suggested as for ^{99m}Tc-MDP TPBS, with the additional presence of a periprosthetic margin of lucency more than 2 mm in width on CT component corresponding to the region of delayed uptake.

The true-positive rate, true-negative rate, false-positive rate, and false-negative rate, sensitivity, and specificity for each modality in the detection of either of these pathologies were calculated among all patients where a final diagnosis of aseptic loosening or periprosthetic infection could be made or definitively excluded. McNemar's test was performed to determine whether there was a significant difference in outcomes of ^{99m}Tc-MDP TPBS and ^{99m}Tc-MDP SPECT/CT in the detection of aseptic loosening and periprosthetic infection [data analysis performed using SPSS, version 23.0 (SPSS Inc., Chicago, Illinois, USA). Diagnoses other than aseptic loosening and infection provided by ^{99m}Tc-MDP SPECT/CT were also recorded.

Patients were followed up to establish a final diagnosis based on a combination of histopathological/cytological findings, other imaging findings (e.g. MRI, radiolabelled white blood cell scan), clinical decisions, and management outcomes (including subsequent intraoperative findings). In total, a final diagnosis of aseptic loosening or periprosthetic infection was established or definitively excluded in 41/49 patients.

Results

^{99m}Tc-MDP TPBS versus ^{99m}Tc-MDP SPECT/CT: diagnosing infection or aseptic loosening

In 41 patients, a definitive outcome regarding the presence/absence of aseptic loosening or periprosthetic infection was obtained. Nine patients in total were found to have either aseptic loosening (6/9) or periprosthetic infection (3/9). Table 1 demonstrates the true positive, true negative, false positive, false negative, sensitivity, and specificity for ^{99m}Tc-MDP TPBS and ^{99m}Tc-MDP SPECT/CT, correspondingly, for all 41 patients in the identification of these pathologies.

There was a significant difference in outcomes of ^{99m}Tc-MDP TPBS versus ^{99m}Tc-MDP SPECT/CT in identifying aseptic loosening or periprosthetic infection ($P = 0.016$). ^{99m}Tc-MDP SPECT/CT was able to correctly identify all nine cases of aseptic loosening (Fig. 1) and periprosthetic infection with sensitivity of 100%, whereas ^{99m}Tc-MDP TPBS failed to identify one case of aseptic loosening resulting in a single false negative and sensitivity of 88.9%. However, specificity of ^{99m}Tc-MDP SPECT/CT (75%; 95% confidence interval: 53.3–90.2%) was considerably higher than ^{99m}Tc-MDP TPBS (30%; 95% confidence interval: 11.9–54.3%). Furthermore, in 5/8 true-positive cases identified on ^{99m}Tc-MDP TPBS, the readers reported increased confidence in their diagnosis of aseptic loosening/periprosthetic infection when reviewing the ^{99m}Tc-MDP SPECT/CT studies. In addition, fewer studies were considered indeterminate when reviewing the ^{99m}Tc-MDP SPECT/CT rather than ^{99m}Tc-MDP TPBS alone.

Incremental value of ^{99m}Tc-MDP SPECT/CT over ^{99m}Tc-MDP TPBS in identifying alternative diagnoses

Aside from aseptic loosening and periprosthetic infection, several other findings were identified on ^{99m}Tc-MDP SPECT/CT as potential pain generators that were not identified on ^{99m}Tc-MDP TPBS (Figs 2 and 3). These are summarized in Table 2.

Alternative diagnoses were identified in a total of 21/49 (43%) patients on ^{99m}Tc-MDP SPECT/CT, which were not detected on review of the ^{99m}Tc-MDP TPBS alone. The most commonly detected alternative diagnosis was degenerative change, particularly at the patellofemoral joint, which was identified in a total of 13 (26.5%) patients, and considered the primary pain generator in 9/10 of these patients where sufficient follow-up information was available to confirm the diagnosis. Increased tracer uptake related to altered biomechanical stress was considered the primary pain generator in three patients. Periprosthetic fracture was identified in two patients, although in one of these patients, this was identified in the presence of periprosthetic infection, hence was not considered the primary pain generator in this case. Heterotopic ossification was identified in a total of two patients, although in the one patient where follow-up information was available, this did not correlate with the site of the patient's pain and was not considered a significant pain generator.

Table 1 ^{99m}Tc-MDP TPBS versus ^{99m}Tc-MDP SPECT/CT in diagnosing infection and aseptic loosening

	^{99m}Tc-MDP TPBS	^{99m}Tc-MDP SPECT/CT
True positive	8	9
False positive	14	6
True negative	6	18
False negative	1	0
Indeterminate	12	8
Sensitivity (%, 95% CI)	88.9, 951.8–99.7%	100, 66.4–100%
Specificity (%, 95% CI)	30, 11.9–54.3%	75, 53.3–90.2%

CI, confidence interval; SPECT/CT, single-photon emission computed tomography/computed tomography; ^{99m}Tc-MDP, technetium-99m-methylene diphosphonate; TPBS, two-phase bone scan.

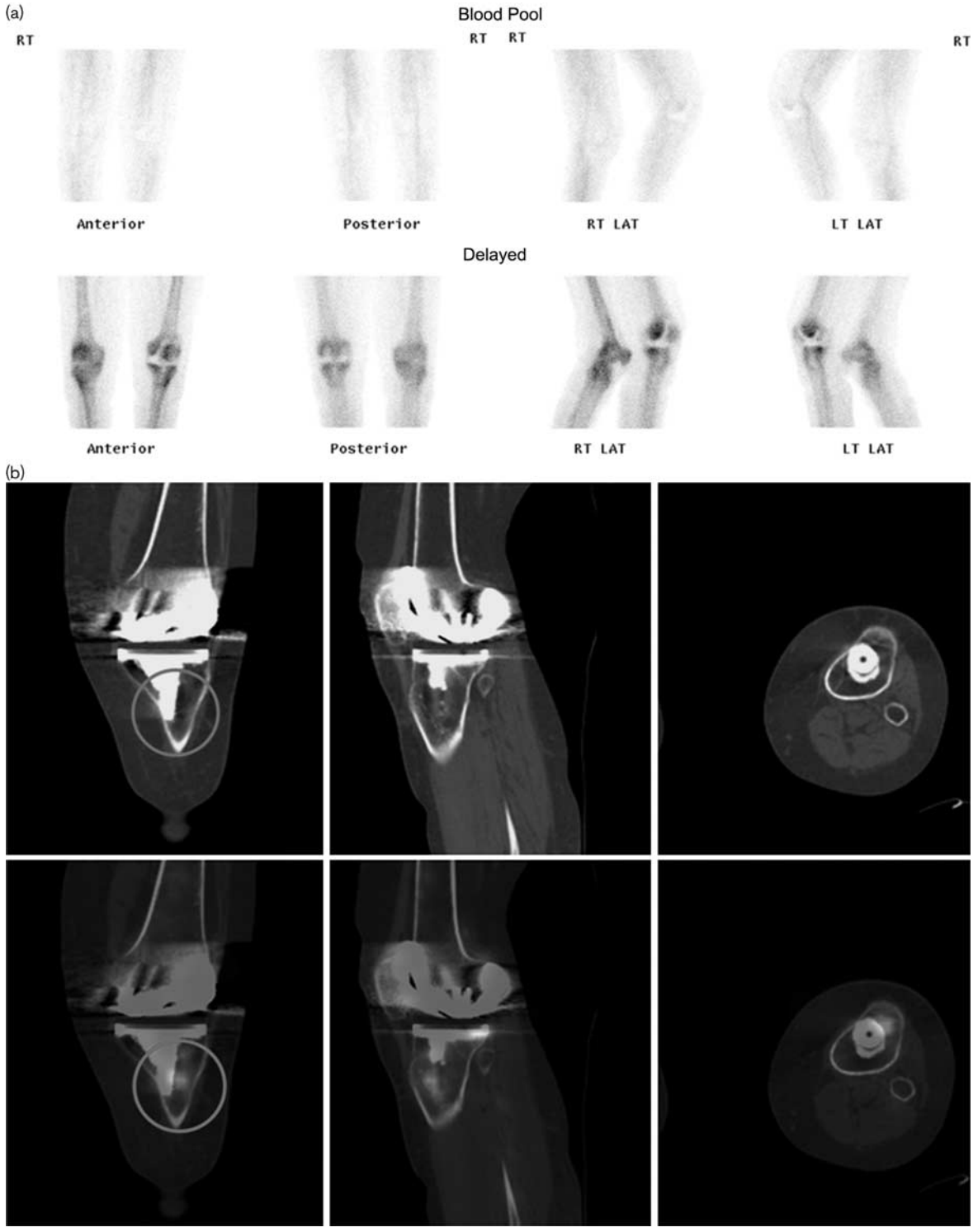
Discussion

This study demonstrates that ^{99m}Tc-MDP SPECT/CT has better sensitivity (100 vs. 88.9%) and specificity (75 vs. 30%) compared with ^{99m}Tc-MDP TPBS in diagnosis of aseptic loosening and periprosthetic infection in patients with painful knee arthroplasty. In addition, ^{99m}Tc-MDP SPECT/CT provided alternative diagnosis of pain generator in 43% of patients, not identified by ^{99m}Tc-MDP TPBS.

Investigation of post-KA knee pain has long posed a significant diagnostic dilemma, owing to (i) the multitude of potential pain generators, (ii) the inherent limitations of conventional radiological modalities in identifying the cause of pain in the presence of extensive metallic prostheses, and (iii) vastly differing optimal management depending on cause. This is perhaps no more important than in the context of periprosthetic infection and aseptic loosening, as both will typically require very differing management options. Planar bone scintigraphy has long been used as part of the diagnostic workup to add metabolic information alongside conventional radiological modalities given its widespread availability and low cost. However, ^{99m}Tc-MDP SPECT/CT has been gaining favor in recent years among referrers.

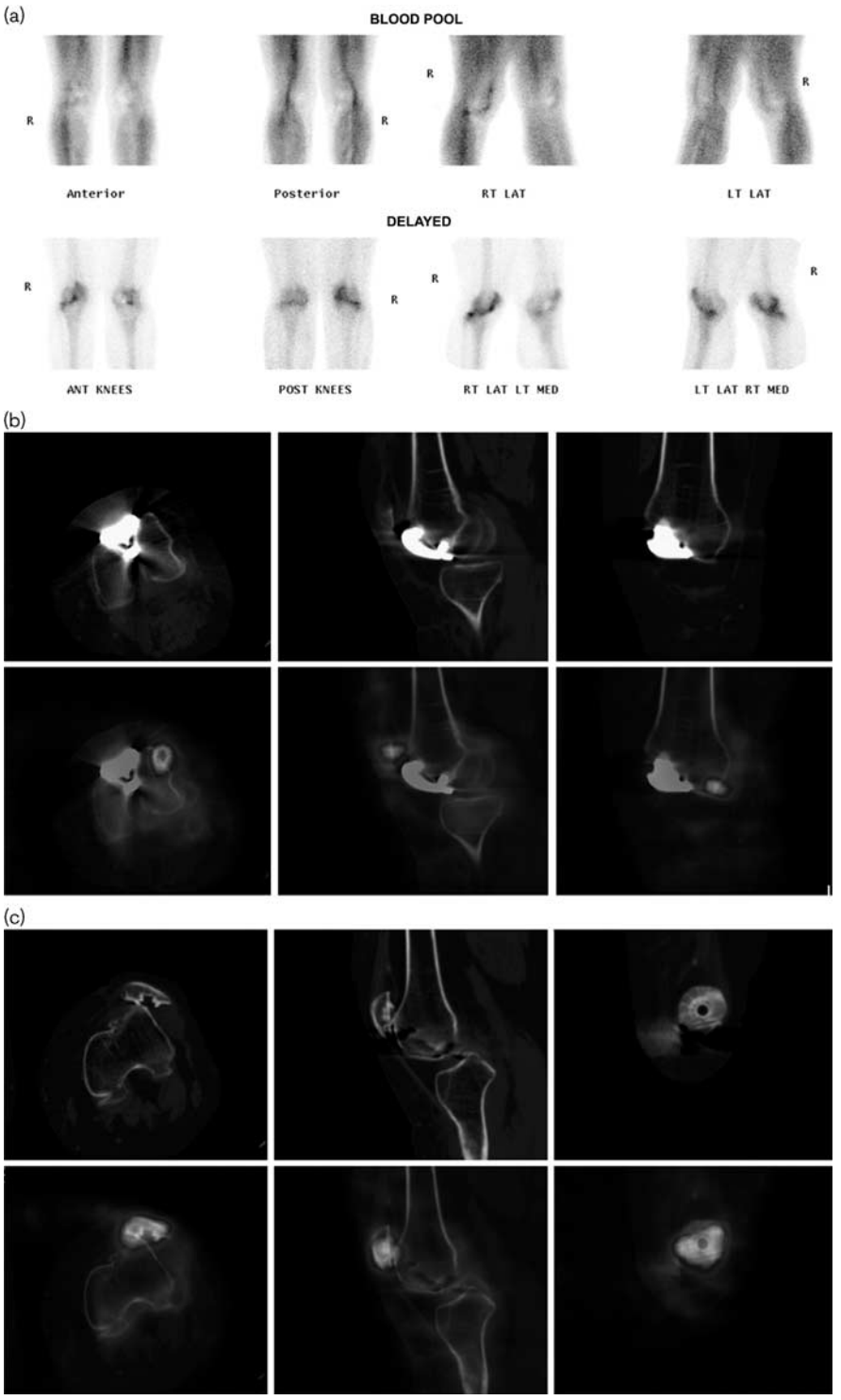
Our findings of high sensitivity but poor specificity of ^{99m}Tc-MDP TPBS in identification of periprosthetic infection and aseptic loosening after KA are in line with previous studies, including a recent meta-analysis comprising two-phase and three-phase planar bone scans, which identified an overall specificity of 56% in the detection of periprosthetic infection [14–18]. Like our study, these studies were based on qualitative assessment of bone scans. There has been one retrospective study of 31 patients following KA, where quantitative assessment of planar bone scans using regions of interest was found to identify aseptic loosening with a sensitivity of 90% and specificity of 100% [19]. However, other similar studies

Fig. 1



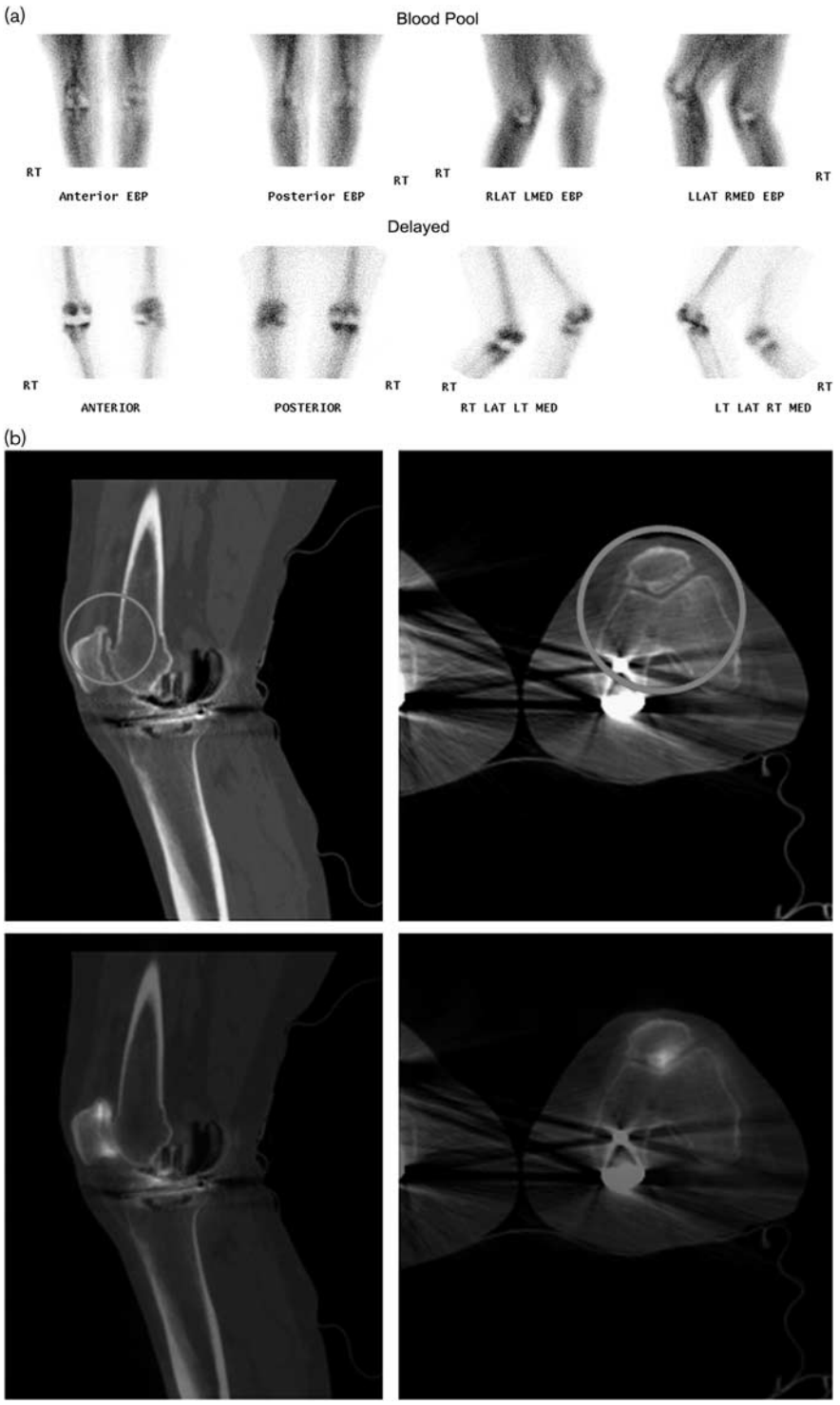
A 79-year-old female with painful left total knee arthroplasty presented 10 years after surgery. (a) There is no significantly abnormal uptake of tracer in the left knee in blood pool and delayed phases of ^{99m}Tc-MDP TPBS. (b) SPECT/CT of the left knee shows minor lucency surrounding the tibial component of the prosthesis on CT with associated increased low-grade uptake of tracer on SPECT (circled), suggestive of loosening. SPECT/CT was helpful in identification of potential pain generator in a negative planar bone scan result. SPECT/CT, single-photon emission computed tomography/computed tomography; ^{99m}Tc-MDP, technetium-99m-methylene diphosphonate; TPBS, two-phase bone scan.

Fig. 2



A 44-year-old female with history of left unicompartmental hemiarthroplasty 8 years ago presented with painful left knee. (a) ^{99m}Tc-MDP TPBS demonstrates no significant increase in tracer uptake in the left knee in blood pool and delayed phase. Increased tracer uptake is noted in the right knee, likely to be degenerative changes. (b) SPECT/CT of the left knee shows no abnormal tracer uptake surrounding the prosthesis. However, mild focal uptake is noted along the lateral condylar margin of the left femur. This is likely to be owing to repetitive impact or subluxation and could be the pain generator. (c) SPECT/CT of the left knee also shows increased tracer uptake in the laterally dislocated patella, which could also be the etiology of pain in the present scenario. Moreover, planar bone scan could not reveal any useful information relevant to cause of pain. SPECT/CT, single-photon emission computed tomography/computed tomography; ^{99m}Tc-MDP, technetium-99m-methylene diphosphonate; TPBS, two-phase bone scan.

Fig. 3



A 62-year-old female with left unicompartmental and recent right total knee arthroplasty presented with pain in the left knee. (a) ^{99m}Tc-MDP TPBS shows no significant abnormal tracer uptake in the left knee on in blood pool and delayed phases. Increased tracer uptake in the right tibial condyles is likely owing to recent postoperative changes. (b) SPECT/CT of the left knee shows increased tracer uptake centered on the degenerative changes at the left patellofemoral joint (circled), suggestive of pain generator. In this example, SPECT/CT is helpful in identification of alternative causes of pain whereas planar bone scan showed no significant pathology. SPECT/CT, single-photon emission computed tomography/computed tomography; ^{99m}Tc-MDP, technetium-99m-methylene diphosphonate; TPBS, two-phase bone scan.

Table 2 ^{99m}Tc-MDP SPECT/CT in identification of alternative diagnoses

Alternative diagnosis	Total number of patients ($n = 21$)	Considered the pain generator at follow-up?		
		Yes	No	Insufficient follow-up to confirm ^{99m}Tc-MDP SPECT/CT findings
Heterotopic ossification	2	0	1	1
Altered biomechanical stress	4	3	0	1
Periprosthetic fracture	2	1	1	0
Degenerative patellofemoral disease	13	9	1	3

SPECT/CT, single-photon emission computed tomography/computed tomography; ^{99m}Tc-MDP, technetium-99m-methylene diphosphonate.

have shown poor reproducibility regarding quantitative analysis of planar bone scans using regions of interest [20].

We have demonstrated a significant difference in outcome and higher specificity of ^{99m}Tc-MDP SPECT/CT versus ^{99m}Tc-MDP TPBS regarding identification of periprosthetic infection and aseptic loosening. Our findings support those of a recent study of 30 KA patients with confirmed aseptic loosening or periprosthetic infection who had undergone previous primary and revision KA and were investigated with ^{99m}Tc-MDP SPECT/CT [21]. This study compared the findings of ^{99m}Tc-MDP three-phase planar bone scan/SPECT versus^{99m}Tc-MDP SPECT/CT in patients with confirmed periprosthetic infection or aseptic loosening and demonstrated significantly superior detection with^{99m}Tc-MDP SPECT/CT [21].

In addition, our study has demonstrated the incremental value of ^{99m}Tc-MDP SPECT/CT in identifying additional potential etiologies of post-KA pain in 43% of patients, which could not be appreciated on ^{99m}Tc-MDP TPBS alone. In particular, we found evidence of patellofemoral degenerative change in 26.5% of patients, which was not identified on ^{99m}Tc-MDP TPBS (Fig. 3); this was considered the primary cause of the pain among 90% of these patients where definitive follow-up information was available. These additional findings exemplify the value of ^{99m}Tc-MDP SPECT/CT in not only identifying various etiologies of post-KA pain but also its ability to distinguish whether a particular pathology is a true pain generator based on the degree of tracer uptake. Our findings are in line with other studies that have demonstrated the value of ^{99m}Tc-MDP SPECT/CT in identifying the active pain generators, including one study where ^{99m}Tc-MDP SPECT/CT altered the working diagnosis in 19/23 (83%) of post-KA patients [22]. A more recent study of 100 KAs similarly showed that ^{99m}Tc-MDP SPECT/CT altered the working diagnosis and final treatment in 85% of cases, with 97% correlation with intraoperative findings in patients who went on to have surgery [8]. Moreover, in line with our findings, this study identified progressive patellofemoral degenerative change as the primary cause of pain in 19% of patients [8].

Although the superiority of ^{99m}Tc-MDP SPECT/CT over ^{99m}Tc-MDP TPBS is perhaps intuitive given the inherent advantages of combined functional and anatomical data, it is nevertheless an important point to demonstrate given that there remains no definitive consensus on the optimal means of investigating and imaging the painful knee post-KA. Indeed, our findings confirm that planar bone scans, without additional SPECT/CT component, should be considered obsolete in the assessment of patients with post-KA knee pain when SPECT/CT is available. Moreover, although the specificity of ^{99m}Tc-MDP SPECT/CT is considerably higher compared with planar studies (75 vs. 30%), it is still suboptimal. As such, complementary tests such as radiolabelled white blood cell scans along with bone marrow studies should be considered to improve accuracy, whenever there is diagnostic doubt.

One group has recently proposed a diagnostic algorithm for investigation of post-KA knee pain suggesting the use ^{99m}Tc-MDP SPECT/CT as the primary imaging modality to be performed following radiographic assessment when clinical findings indicate that the source of pain is localized to the knee [23]. The same group has proposed a standardized SPECT/CT algorithm incorporating a mapping scheme for tracer localization, incorporation of normalized bone tracer uptake values (measured against background uptake at the mid femoral shaft), and 3D analysis of prosthesis position and alignment with near perfect interobserver and intraobserver agreement [23,24]. By using this mapping scheme in a recent study of 37 patients with bilateral KA with unilateral knee pain, the same group showed that symptomatic KAs are associated with significantly greater internal rotation of the prostheses compared with asymptomatic KAs [25]. The same study also showed that the highest tracer uptake among both symptomatic and asymptomatic KAs was around the tibial stem, although symptomatic KAs were associated with greater intensity of bone tracer uptake.

Typical routine interpretation of ^{99m}Tc-MDP SPECT/CT in the post-KA knee in most centers (including our own) is based on qualitative assessment of 2D and 3D reconstructions of SPECT and CT data. Although this qualitative approach can perhaps be considered a limitation in our study, the fact that it is representative of most reporting practices highlights the relevance of our findings in current routine clinical practice. Future directions should, however, focus on quantitative methods that incorporate 3D component position and normalized bone tracer uptake values. This will provide a more robust

and reproducible approach to image interpretation to further develop our understanding of pathology-specific patterns of component position, tracer uptake, and tracer intensity.

Conclusion

^{99m}Tc-MDP SPECT/CT has better sensitivity and specificity compared with ^{99m}Tc-MDP TPBS in diagnosis of aseptic loosening and periprosthesis infection in patients with painful knee arthroplasty. ^{99m}Tc-MDP SPECT/CT provided alternative diagnosis of pain generator in 43% of patients, not identified by ^{99m}Tc-MDP TPBS.

Acknowledgements

The authors thank Dr D. Prezzi, Department of Radiology, Guy's and St Thomas' NHS Foundation Trust for assistance in statistical analysis.

Conflicts of interest

There are no conflicts of interest.

References

1 Steiner C, Andrews R, Barrett M, Weiss A. *HCUP projections: mobility/orthopedic procedures 2003 to 2012 HCUP Projections Report #2012-03*. Rockville, MD: Agency for Healthcare Research and Quality; 2012. Available at: *http://hcup-us.ahrq.gov/reports/projections/2012-03.pdf*. [Accessed 7 June 2017].
2 MaraditKremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, *et al*. Prevalence of total hip and knee replacement in the United States. *J Bone Joint Surg Am* 2015; **97**:1386–1397.
3 Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89**:780–785.
4 Mannion AF, Kämpfen S, Munzinger U, Kramers-de Quervain I. The role of patient expectations in predicting outcome after total knee arthroplasty. *Arthritis Res Ther* 2009; **11**:R139.
5 Becker R, Bonnin M, Hofmann S. The painful knee after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**:1409–1410.
6 Hirschmann MT, Henckel J, Rasch H. SPECT/CT in patients with painful knee arthroplasty-what is the evidence? *Skeletal Radiol* 2013; **42**:1201–1207.
7 Mandalia V, Eyres K, Schranz P, Toms AD. Evaluation of patients with a painful total knee replacement. *J Bone Joint Surg Br* 2008; **90**:265–271.
8 Hirschmann MT, Amsler F, Rasch H. Clinical value of SPECT/CT in the painful total knee arthroplasty (TKA): a prospective study in a consecutive series of 100 TKA. *Eur J Nucl Med Mol Imaging* 2015; **42**:1869–1882.
9 Park CN, White PB, Meftah M, Ranawat AS, Ranawat CS. Diagnostic algorithm for residual pain after total knee arthroplasty. *Orthopedics* 2016; **39**:e246–e252.
10 McDowell M, Park A, Gerlinger TL. The painful total knee arthroplasty. *Orthop Clin North Am* 2016; **47**:317–326.
11 Gehrke T, Alijanipour P, Parvizi J. The management of an infected total knee arthroplasty. *Bone Joint J* 2015; **97B**:20–29.
12 Fritz J, Lurie B, Potter HG. MR imaging of knee arthroplasty implants. *Radiographics* 2015; **35**:1483–1501.
13 Mulcahy H, Chew FS. Current concepts in knee replacement: features and imaging assessment. *Am J Roentgenol* 2013; **201**:W828–W842.
14 Vaz S, Ferreira TC, Salgado L, Paycha F. Bone scan usefulness in patients with painful hip or knee prosthesis: 10 situations that can cause pain, other than loosening and infection. *Eur J Orthop Surg Traumatol* 2017; **27**:147–156.
15 Ouyang Z, Li H, Liu X, Zhai Z, Li X. Prosthesis infection: diagnosis after total joint arthroplasty with three-phase bone scintigraphy. *Ann Nucl Med* 2014; **28**:994–1003.
16 Claassen L, Ettinger M, Plaass C, Daniilidis K, Calliess T, Ezechieli M. Diagnostic value of bone scintigraphy for aseptic loosening after total knee arthroplasty. *Technol Health Care* 2014; **22**:767–773.
17 Verberne SJ, Sonnega RJ, Temmerman OP, Raijmakers PG. What is the accuracy of nuclear imaging in the assessment of peri-prosthetic knee infection? A meta-analysis. *Clin Orthop Relat Res* 2017; **475**:1395–1410.
18 Ryd L, Gustafson T, Lindstrand A. ^{99m}Tc-diphosphonate scintigraphy in successful knee arthroplasty and its relation to micromotion. *Clin Orthop Relat Res* 1993; **287**:61–67.
19 Klett R, Steiner D, Laurich S, Bauer R, Kordelle J. Evaluation of aseptic loosening of knee prostheses by quantitative bone scintigraphy. *Nuklearmedizin* 2008; **47**:163–166.
20 Sacchetti GM, Ghisellini F, Brambilla M, de Consoli A, Fornara P, Rizzo E, *et al*. Quantitative scintigraphic evaluation of total knee arthroplasties: a feasibility study. *Clin Orthop Relat Res* 1996; **325**:181–189.
21 Arıcan P, Okudan Tekin B, Şefizade R, Naldöken S, Baştuğ A, Özkurt B. The role of bone SPECT/CT in the evaluation of painful joint prostheses. *Nucl Med Commun* 2015; **36**:931–940.
22 Hirschmann MT, Konala P, Iranpour F, Kerner A, Rasch H, Friederich NF. Clinical value of ^{99m}Tc-HDP-SPECT-CT for assessmentof patients with painful knees after total knee arthroplasty – a new dimension of diagnostics. *BMC Musculoskelet Disord* 2011; **12**:36.
23 Rasch H, Falkowski AL, Forrer F, Henckel J, Hirschmann MT. 4D SPECT/CT in orthopaedics: a new method of combined quantitativevolumetric 3D analysis of SPECT/CT tracer uptake and componentposition measurements in patients after total knee arthroplasty. *Skeletal Radiol* 2013; **42**:1215–1223.
24 Hirschmann MT, Wagner CR, Rasch H, Henckel J. Standardized volumetric 3D-analysis of SPECT/CT imaging in orthopaedics: overcoming the limitations of qualitative 2D analysis. *BMC Med Imaging* 2012; **12**:5.
25 Awengen R, Rasch H, Amsler F, Hirschmann MT. Symptomatic versus asymptomatic knees after bilateral total knee arthroplasty: what is the difference in SPECT/CT? *Eur J Nucl Med Mol Imaging* 2016; **43**:762–772.